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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,192	12/31/2003	Pei Kan	KANP3002/REF/LES	5546
23364 7590 03/16/2011 BACON & THOMAS, PLLC 625 SLATERS LANE FOURTH FLOOR ALEXANDRIA, VA 22314-1176			EXAMINER HOLLOMAN, NANETTE	
			ART UNIT	PAPER NUMBER
			1612	
			MAIL DATE	DELIVERY MODE
			03/16/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/748,192

Applicant(s)

KAN ET AL.

Examiner

NANNETTE HOLLOMAN

Art Unit

1612

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 December 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

This Office Action is in response to the Request for Continued Examination filed on December 7, 2010. Applicants' arguments, filed December 7, 2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Action is made Final.

Claim Rejections - 35 USC § 103

1) Claims 1-21 and 23-24 were rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney 6,632,457) in view of Jeong et al. (US Patent No. 6,841,617). This rejection is maintained.

Applicant's Arguments

Applicant argues Sawhney used oil-in-water-in-oil with macromer polymerized in the outside water phase to form the system. At the same time, some hydrophobic substance may partition to the outside oil phase or accumulate on the outside surfaces of the hydrogel microspheres once the hydrogel microspheres become solid through polymerization. As a result, the outside surface associated hydrophobic substance may release very quickly and result in a burst effect. Applicant further argues the hydrogels of the secondary reference were used alone and a burst effect was shown due to a high percentage of water content in the solidified depot. Applicant argues taken together, the delivery systems based on the references alone cannot avoid the burst effect. Applicant further argues unexpected results. Applicant's arguments filed December 7, 2010 have been fully considered but they are not persuasive.

Examiner's Response

It appears Applicant is arguing the merits of the rejection based upon the disclosure of each reference alone. Jeong is used to disclose why one of ordinary skill in the art would want to modify the teaching of Sawhney and not as a stand alone reference as argued by Applicant. In regard to Sawhney, the reference discloses a controlled release delivery system where the drug release is controlled and sustained, while being free from "burst effects" (column 2, lines 41-44); wherein hydrogel microspheres may be formed from non-polymerized hydrogel forming materials that are stabilized by virtue of their limited solubility, ionic complexation or other means (column 20, lines 34-43). Sawhney discloses a method of suspending an active agent within an

oil phase to form a dispersion; wherein the dispersion may then be emulsified within the hydrogel solution, wherein the active agent would not diffuse to the outer surface during polymerization as Applicant asserts since non-polymerized hydrogel material may be used (column 13, lines 23-33). Furthermore, the oil phase would not be heated to degrade the hydrogel.

In regard to Jeong showing "burst effects", the reference was used to disclose thermogelling polymers, which are considered to meet the limitation of "temperature sensitive" as claimed, that gel *in situ* and are the basis of injectable systems that eliminate the need for surgical procedures and offers the advantage of the ability to form any desired implant shape. This provides the motivation to one of ordinary skill in the art to use such polymers in the compositions of Sawhney. Therefore using the polymers of Jeong would not cause a "burst effect" in the compositions of Sawhney because the drug is entrapped in the oil phase.

In regard to Applicant's unexpected and unique properties as compared to a hydrogel matrix, it is reasonable to conclude that similar results, such as long term sustained release, would occur when using the composition of Sawhney with the thermogelling polymers of Jeong because the combined teachings suggest the composition of the instant claims. Furthermore, Sawhney discloses the desire to extend release of therapeutic agents to several days, weeks, or even months with out the known hydrogel rapid release (column 9, lines 54-62). Therefore, the results do not appear to be unexpected based on the teachings of Sawhney in view of Jeong. Applicant's comparison of examples 9 and 10 in the instant specification does not

appear to be a proper comparison, as the results of FIG. 6A, p. 33 and FIG. 7A, p. 35 are not based on the same scale (Time (day)).

2) Claim 22 was rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney 6,632,457) in view of Jeong et al. (US Patent No. 6,841,617) as applied to claims 1-21 and 23-24, and further in view of Fowers et al. (US Patent No. 6,592,899). This rejection is maintained.

Applicant's Arguments

See Applicant's arguments supra in regard to Sawhney in view of Jeong. Applicant further argues the hydrogels of Fowers were used alone and a burst effect was shown due to a high percentage of water content in the solidified depot. Applicant's arguments filed December 7, 2010 have been fully considered but they are not persuasive.

Examiner's Response

See Examiner's Response supra in regard to Sawhney in view of Jeong. Fowers was used to disclose a copolymer that increases the solubilization capacity and stability of drug solutions thereby enhancing the efficiency and therapeutic effects of the drug, thus providing the motivation to use the copolymer in the system of Sawhney in view of Jeong. Therefore, Fowers is used to disclose why one of ordinary skill in the art would

want to modify the teaching of Sawhney in view of Jeong and not as a stand alone reference as argued by Applicant.

Declaration

The declaration under 37 CFR 1.132 filed December 7, 2010 is insufficient to overcome the rejection of claims 1-21 and 23-24 based upon U.S.C. 103(a) as being unpatentable over Sawhney 6,632,457) in view of Jeong et al. (US Patent No. 6,841,617) as set forth in the last Office action because:

Declarant alleges in the declaration the burst effect must happen in Sawhney's system even if Sawhney's system is combined with Jeong's hydrogel. Applicant further alleges four review papers support the argument that a burst effect always occurs in a polymer microsphere system because drugs may reside on or close to the surface of the microspheres during emulsion-preparation.

Examiner submits that Applicant's references disclose reasons explaining the burst release of polymer microsphere systems. Reference (1) (Yao et al.) discuss initial burst are based on common formulation parameters i.e. increased temperatures to remove solvents. Reference (2) (Freiberg et al.) discuss formation of polymer microspheres by polymerization of the polymer. Reference (3) (Wu et al.) discuss polymer-based sustained-release dosage forms have challenges of protein degradation. Reference (4) (Allison) discuss the initial burst is based on formulation strategies, i.e. removal of solvent. Sawhney discloses the use of solvents causes defects during evaporation, phase inversion and cause problems such as large burst effects (column

17, lines 8-12). Sawhney also discloses proteins and growth factors, which may be denatured by contact with water from the hydrogel environment, first may be lyophilized and suspended within an oil phase to form a dispersion that create a microenvironment that not only stabilizes the molecules but also controls their release rate (column 13, lines 23-37). Therefore, it appears Sawhney addresses the concerns of the references by providing alternant formation parameters which would deter the burst release of the prior art.

Action is Final

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANNETTE HOLLOMAN whose telephone number is (571)270-5231. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/N. H./
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612